REMARKS

Claims 13, 17, and 19-42 are pending in the application. Claims 13, 17, and 19-38 are withdrawn as being drawn to non-elected inventions. Applicants reserve the right to prosecute the non-elected claims in subsequent divisional applications. Claims 39-42 are currently being examined on the merits.

Claim 39 has been amended to further clarify the intended subject matter of the claimed invention. No new matter is added by this amendment. The present amendment does not introduce any new issues, and places the subject application in condition for allowance and/or simplifies issues for appeal. Accordingly, entry of the amendment is proper and respectfully requested.

Withdrawal of previous rejections

Applicants would like to thank the Examiner for withdrawing previous rejections stated in the last office action. Applicants believe that with the amendments offered in this response and the remarks made herein, the remaining rejections should also be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph:

The rejection of claims 39-42 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite was maintained. The Office Action asserts that claim 39 is rendered vague and indefinite by the recitation of "biologically active fragments" (Office Action, pages 2-3).

Although not acquiescing in the stated reasons for the rejection of claims 39-42 under 35 U.S.C. §112, second paragraph, claim 39 has been amended to obviate this rejection. Therefore, reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph:

The rejection of claims 39 and 41 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement was maintained. Applicants respectfully point out that the Office Action is incorrect in stating that claim 42 is drawn in part to variants of SEQ ID NO:2 (Office Action, page 3, section 6(A)) as only claims 39 and 41 are drawn to variants. The Office Action asserts that neither variants having 90% amino acid sequence identity to SEQ ID NO:2 or biologically active fragments are enabled.

Although not acquiescing in the stated reasons for the rejection of claims 39 and 41 under 35 U.S.C. §112, first paragraph, claim 39 has been amended herein so that it no longer recites biologically active fragments of SEQ ID NO:2. Thus the rejection as it pertains to this portion of the claims is moot.

With respect to the claimed variants, the Office Action asserts that "the specification does not identify variants of SEQ ID NO:2 that would be expressed on the surface of stem cells, or the organs or tissues which would have said stem cells" (Office Action, page 3). The Office Action further asserts that "the specification does not provide a written description of the amino acid sequences of the claimed variants to SEQ ID NO:2" (Office Action, page 3). Thus the rejection appears to be for both written description and enablement, although the Office Action does not explicitly state this. Accordingly, both issues are addressed below.

1. Written description rejection under 35 U.S.C. § 112, first paragraph:

A. Legal Requirements

The requirements necessary to fulfill the written description requirement of 35 § U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.

B. The Specification provides an adequate written description of the claimed "variants" of SEQ ID NO:2.

The subject matter recited in amended claim 39 is adequately disclosed in the Specification given what is conventional or well known to one skilled in the art.

SEQ ID NO:2 is specifically disclosed in the application (see, for example, Figure 2). Variants of SEQ ID NO:2 are described, for example, at page 4, lines 25-33 and page 10, line 28 through page 11, line 3. Chemical and structural features of SEQ ID NO:2 are described, for example, at page 6, lines 5-19. Given SEQ ID NO:2, one of ordinary skill in the art would recognize variants of SEQ ID NO:2 having 90% sequence identity to SEQ ID NO:2.

Furthermore, the specification has also disclosed residues which are conserved across a number of stem cell antigens and thus likely to be important for function, for example, the conserved cysteine residues (specification, page 6, lines 15-19). Applicants also note that it is well-known in the art that members of the Ly-6 stem cell antigen family are anchored to the cell membrane by a GPI anchor (specification, p. 1, lines 11-13). Ly-6 family members are known to have C-terminal hydrophobic signal sequences for GPI attachment (see the Classon reference, submitted with the Response to Office Action mailed October 15, 2002, at page 5298, col. 1). The C-terminus of SCAH-2 is enriched in hydrophobic amino acids as shown in a hydrophobicity plot for SCAH-2 (specification, Figure 5), indicating that it too contains this characteristic C-terminal hydrophobic sequence. Thus the skilled artisan would have additional guidance in making and using the claimed variants. Specific tissues in which scah sequences were found to be expressed, including bladder, breast, lung, ovary, prostate and uterus, are identified in the specification (specification, page 24, lines 14-18). In addition, assays for determining the presence and distribution of SCAH-2 molecules in cell populations are described in the specification at, for example, page 38, lines 10-12. Assays to determine functional activity are considered routine experimentation when identifying functional sequence variants.

One of ordinary skill in the art would recognize polypeptide sequences which are variants having at least 90% amino acid identity to SEQ ID NO:2, as those polypeptide sequences which, when assayed, have the stem cell antigen activity of being expressed on the surface of stem cells. Thus, polypeptides comprising an amino acid sequence that is 90% identical to the amino acid sequence of SEQ ID NO:2 can easily be identified by one of skill in the art based on both the presence of functional and structural domains and by the assay, all disclosed in the specification.

C. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant phasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular

DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polypeptides in terms of chemical structure, in addition to functional characteristics. For example, the "variant language" of independent claim 39 recites chemical structure to define the claimed genus:

> 39. A purified polypeptide comprising an amino acid sequence selected from the group consisting of:
>
> a) an amino acid sequence of SEQ ID NO:2,
>
> b) an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:2, wherein said amino acid sequence is expressed on the surface of stem cells...

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:2. In the present case, there is no reliance merely on a description of functional characteristics of the polypeptides recited by the claims. Moreover, the functional recitations included only add to the structural characterization of the recited polypeptides. The polypeptides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

Accordingly, Applicants have disclosed the claimed invention in sufficient detail and provided identifying characteristics such that the skilled artisan would understand that Applicants were in possession of the claimed invention. Therefore, reconsideration and withdrawal of this rejection to the claims are respectfully requested.

2. Enablement rejection under 35 U.S.C. § 112, first paragraph:

To fulfill the enablement requirement of 35 U.S.C. §112, first paragraph, the claimed invention must be described in the specification in such as way as to enable one skilled in the relevant art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner is well aware that relative skill of those in the art is very high and the amount of direction or guidance needed to be disclosed in the specification is that required to make and use the variants of SEQ ID NO:2 as claimed.

The Office Action does not dispute that SEQ ID NO:2 has utility and is enabled. The claimed variants share the utilities of SEQ ID NO:2, for example in disease diagnosis, expression profiling, and drug discovery (specification, page 18, lines 7-17; page 20, lines 5-19; page 20, line 32 though page 21, line 17; and pages 21-24). Thus one of ordinary skill in the art would clearly understand how to use the claimed variants.

Furthermore, the specification has also disclosed residues which are conserved across a number of stem cell antigens and thus likely to be important for function, for example, the conserved cysteine residues (specification, page 6, lines 15-19). Applicants also note that it is well-known in the art that members of the Ly-6 stem cell antigen family are anchored to the cell membrane by a GPI anchor (specification, p. 1, lines 11-13). Ly-6 family members are known to have C-terminal hydrophobic signal sequences for GPI attachment (see the Classon reference, submitted with the Response to Office Action mailed October 15, 2002, at page 5298, col. 1). The C-terminus of SCAH-2 is enriched in hydrophobic amino acids as shown in a hydrophobicity plot for SCAH-2 (specification, Figure 5), indicating that it too contains this characteristic C-terminal hydrophobic sequence. Thus the skilled artisan would have ample guidance in making the claimed variants.

Applicants further note that the specification does identify specific tissues in which scah sequences were found to be expressed, including bladder, breast, lung, ovary, prostate and uterus (specification, page 24, lines 14-18). Thus one of ordinary skill in the art would be able to determine the bodily tissues from which to isolate the stem cells without any undue experimentation. In addition, assays for determining the presence and distribution of SCAH-2 molecules in cell populations are described in the specification at, for example, page 38, lines 10-12. Assays to determine functional activity are considered routine experimentation when identifying functional sequence variants.

Applicants also respectfully point out that there are methods of isolating variants of SEQ ID NO:2 that do not require isolation of any stem cells. For example, one of skill in the art would understand how to generate variant SCAH-2 sequences from SEQ ID NO:2 or SEQ ID NO:4 using

the techniques disclosed at, for example, page 11, lines 12-17, and page 12, lines 4-6, and using the guidance provided by the specification to determine what changes to make (specification at, for example, page 4, lines 30-33, and page 10, line 30 through page 11, line 3) and to assay the variants for function (specification, page 38, lines 10-12). As discussed above, the specification discloses residues and regions likely to be important for function, such as the conserved cysteine residues and the C-terminal hydrophobic anchor sequence.

The skilled artisan would also understand how to use SEQ ID NO:4, encoding SCAH-2, to detect polynucleotides that encode variants of SCAH-2 from genomic DNA (specification, page 26, line 20 through page 27, line 5). The skilled artisan would further understand how to search a nucleotide or protein database for sequences having at least 90% identity to SEQ ID NO:2 using methods such as BLAST (specification, page 33, lines 25-31). The variants identified by any of these methods could be tested using the disclosed assay (specification, page 38, lines 10-12) to determine whether they have the activity recited by the claims. One of skill in the art would know which types of stem cells to test the isolated variants in by following the guidance in the specification as to which tissues SCAH-2 is expressed in (specification, page 24, lines 14-18). Thus the Office Action's assertions regarding the possibility of determining the correct tissues from which to isolate variants are not relevant, as one of skill in the art would readily understand that there are methods to isolate the claimed variants that do not require starting with any specific tissue or stem cell.

> In addition, as set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):
>
> The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Contrary to the standard set forth in *Marzocchi*, the Office Action has failed to provide any ***reasons*** why one would doubt that the guidance provided by the present Specification would enable

one to make and use the recited variants of SEQ ID NO:2. Hence, a *prima facie* case for non-enablement has not been established with respect to the recited variants of SEQ ID NO:2.

Accordingly, for all the above reasons, the claimed subject matter is described in the Specification in such a way that one skilled in the art can make and/or use the claimed invention. Therefore, reconsideration and withdrawal of this rejection to the claims are respectfully requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney/Agent below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**, as set forth in the enclosed fee transmittal letter.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 39 has been amended as follows:

39. **(Thrice Amended.)** A purified polypeptide comprising an amino acid sequence selected from the group consisting of:

a) an amino acid sequence of SEQ ID NO:2,

b) an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:2, wherein said amino acid sequence is expressed on the surface of stem cells, and

c) [a biologically-active fragment of the amino acid sequence of SEQ ID NO:2, wherein said biologically-active fragment is expressed on the surface of stem cells, and

d)] an immunogenic fragment of the amino acid sequence of SEQ ID NO:2, wherein said immunogenic fragment comprises at least 5 contiguous amino acids of SEQ ID NO:2 and is capable of generating an antibody that specifically binds to the polypeptide encoded by SEQ ID NO:2.